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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/675,852	09/30/2003	Jacqueline E. Heard	MBIO-001/84US 132976-2004	1145

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EXAMINER	
KRUSE, DAVID H	

ART UNIT	PAPER NUMBER
1638	

MAIL DATE	DELIVERY MODE
11/14/2011	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/675,852	HEARD ET AL.	
	Examiner	Art Unit	
	DAVID H. KRUSE	1638	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 September 2011*.

2a)☐ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ An election was made by the applicant in response to a restriction requirement set forth during the interview on _____; the restriction requirement and election have been incorporated into this action.

4)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

5)☒ Claim(s) *85-98* is/are pending in the application.

5a) Of the above claim(s) _____ is/are withdrawn from consideration.

6)☐ Claim(s) _____ is/are allowed.

7)☒ Claim(s) *85-98* is/are rejected.

8)☐ Claim(s) _____ is/are objected to.

9)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

10)☐ The specification is objected to by the Examiner.

11)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

12)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

STATUS OF THE APPLICATION

1. This Office action is in response to the Amendment and Remarks filed on 14 September 2011.

Priority

2. Applicant's claim for the benefit of a prior-filed application under 35 U.S.C. 119(e) or under 35 U.S.C. 120, 121, or 365(c) is acknowledged. Applicant has not complied with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. 119(e) as follows: The later-filed application must be an application for a patent for an invention which is also disclosed in the prior application (the parent or original non-provisional application or provisional application). The disclosure of the invention in the parent application and in the later-filed application must be sufficient to comply with the requirements of the first paragraph of 35 U.S.C. 112. See *Transco Products, Inc. v. Performance Contracting, Inc.*, 38 F.3d 551, 32 USPQ2d 1077 (Fed. Cir. 1994). Applicants' arguments filed on 14 September 2011 have been fully considered but not found to be persuasive.

The instant claims are directed to SEQ ID NO: 4, encoded by SEQ ID NO: 3. As previously discussed U.S. Provisional Application 60/125,814 filed 23 March 1999 does not adequately support the instant claims under 35 U.S.C. 112, first paragraph. U.S. Provisional Application 60/125,814 does not describe the claimed method steps as they relate directly to instant SEQ ID NO: 4.

Applicants argue that their disclosure in US Provisional patent no. 60/125,814 that the sequences provided therein may be transformed into plants to affect their

phenotype e.g., claims 1 and 2, to provide useful traits: "In one aspect, the invention provides a recombinant construct which when introduced in a plant alters the phenotype of the plant. Of particular interest, are changes in seed phenotype. Desirable changes in a seed's phenotype include its germination characteristics; shelf-life; drydown characteristics; size; stress responses, such as to heat, cold, *salt or osmotic shock;* protein, oil or starch content; other nutritional content, such as vitamins, minerals, flavonoids, phytosterols or phytic acid; seedling vigor; insect resistance, seed coat quality or the like. Alternatively, the changes may occur in fruit, seeds, roots, flowers, leaves, shoots, seedlings or in combinations of such tissue. And desirable phenotypic changes include increased pest or insecticide resistance, increased plant biomass, resistance to environmental stresses or the like" (60/125,814, beginning at page 1, line 30, *emphasis* added).

Applicants argue that Y13724 present in 60/125,814 is the same sequence found in Edwards (Y13724) is indicated as AtHAP3b in Edwards in Fig. 3 in the right-most column), a reference cited against Applicants.

Applicants argue that the sequences, plants, traits, and utility that describe the present invention, that the same sequence, Y13724, is found in the art and priority application 60/125,814, that the latter disclosure provides utility for the sequence and plants transformed with it, and that the date of the art and the priority of the instant application are is less than one year after the cited art (page 4, Item 7, of the Remarks).

This is not found persuasive because the sequence in 60/125,814 is not SEQ ID NO: 4; the sequence has amino acids not in SEQ ID NO: 4 at the N- and C-termini and

only comprise amino acids 5-190 of SEQ ID NO: 4. Thus, plants comprising Edwards' sequence were not described in 60/125,814. The provisional application does not make a structure-function correlation for a method of producing and selecting a transgenic plant exhibiting greater salt or osmotic stress tolerance as presently claimed. A list of likely characteristics one would look for is not an adequate description for the instantly claimed methods.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 85, 86, 88, 89, 91-94, 97 and 98 remain rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This rejection is repeated for the reason of record as set forth in the last Office action mailed 15 April 2011. Applicant's arguments filed 14 September 2011 have been fully considered but they are not persuasive.

Applicants claim method of making a transgenic seedling or more mature plant comprising a recombinant polynucleotide encoding a polypeptide that is at least 95-98% identical to SEQ ID NO: 4.

Applicants describe a transgenic plant comprising a recombinant polynucleotide encoding instant SEQ ID NO: 4 operably lined to a constitutive CaMV 35S promoter that are more tolerant to high NaCl (salt) in a germination assay than an equivalent non-transformed plant (see Table 6, page 95 of the instant Specification).

Applicants do not describe recombinant polynucleotides or plants transformed therewith, that confer tolerance to salt or osmotic stress that encodes a polypeptide that is at least 95-98% identical to SEQ ID NO: 4.Hence, it is unclear that Applicants were in possession of the invention as broadly claimed. It was recognized in Swindell et al. (2007) "The biological limitations of transcriptomics in elucidating stress and stress responses." *Heredity* 99: 143-150, that "[c]andidate genes *with a well-supported role in stress-response pathways* provide good prospects for subsequent experimental study" *(emphasis* added; page 149, left column), but "[t]he identification of temperature-related genes [i.e., regulated in response to environmental changes] through microarray analysis represents *only a first step* towards understanding their role in cold- and heat-stress- regulatory *pathways"(emphasis* added; page 149, left column). Given the nature of the art of the instantly claimed invention, Applicants' burden to show possession of the invention as broadly claimed would be substantial given what those skilled in the art would view as being in Applicants' possession based on the description of the claimed invention.

Applicants argue that every species encompassed by the claimed invention, however, need not be disclosed in the specification to satisfy the written description requirement of 35 U.S.C. § 112, first paragraph. *Utter v. Hiraga,* 845 F.2d 993, 6

USPQ2d 1709 (Fed. Cir. 1988). Applicants argue that the Federal Circuit has made it clear that sufficient written description requires simply the knowledge and level of skill in the art to permit one of skill to immediately envision the product claimed from the disclosure. *Purdue Pharm L.P.v. Faulding In.,* 230 F.3d 1320 1323, 596 USPQ2d 1481, 1483 (Fed. Cir. 2000) ("One skilled in the art must immediately discern the limitations at issue in the claims.") (page 5, 2nd paragraph of the Remarks).

Applicants argue that methods for determining percent identity between any two sequences are well-known in the art and are also provided in the instant specification. Applicants argue that having correlated the claimed functions with structures that are sufficiently known or disclosed (e.g., instantly disclosed and art-recognized CCAAT- box binding conserved B domains), the instant claims directed to methods with polypeptides having at least 95% or 98% sequence identity to the amino acid SEQ ID NO: 4 meet the requirements for written description set forth by the Federal Circuit (page 5, 5th paragraph of the Remarks).

These arguments are not found to be persuasive. The Examiner has address the fact that one of skill in the instant art could not envision the genus of encoded amino acid sequences required to practice the claimed method(s). See *University of Rochester v. G.D. Searle & Co.,* 68 USPQ2d 1424, 1433 (DC WNY 2003) which teaches knowing the "starting point" is not enough; that is little more than a research plan. The court held that the disclosure of screening assays and general classes of compounds was not adequate to describe compounds having the desired activity: without disclosure of which peptides, polynucleotides, or small organic molecules have the desired

characteristic, the claims failed to meet the description requirement of § 112. In the instant case, transcription factors were recognized in the instant art as controlling/regulating many genes, and one skilled in the instant art cannot envision what species that are 95-98% identical to instant SEQ ID NO: 4 would regulate salt or osmotic stress tolerance in a plant transformed therewith (see Swindell *et al* 2007 addressed above).

Claim Rejections - 35 USC § 103

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

6. Claims 85-98 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Edwards *et al* (July 1998, Plant Physiology 117: 1015-1022) in view of Harada *et al* (U.S. Patent 6,235,975 B1, filed 24 June 1998) and in further view of Edwards (16 September 1997, Accession No. Y13724, Genbank Sequence, NCBI, National Library of Medicine, National Institutes of Health, Bethesda, MD). This rejection is repeated for the reason of record as set forth in the last Office action mailed 15 April 2011. Applicant's arguments filed 14 September 2011 have been fully considered but they are not persuasive.

Edwards teaches a recombinant polynucleotide encoding the AtHAP3b CAAT-box transcription factor having 874 nucleotides identical to that of Applicant's SEQ ID NO: 3, encoding 188 of 190 amino acids of Applicant's SEQ ID NO: 4. The AtHAP3b

CAAT-box transcription factor taught by Edwards has the "conserved domain" of Applicants' SEQ ID NO: 4. Edwards teaches that expression of the AtHAP3b CAAT-box transcription factor in leaves from plants grown in soil but not in those from liquid culture may suggest environmental regulation of this gene, perhaps in relation to osmotic stress (page 1021, left column, 2nd paragraph). Edwards teaches that further research is required to understand the regulation of this factor and its role in developmental and environmental responses. Edwards 1997 is cited as evidence that the AtHAP3b, CCAAT box binding protein as publicly disclosed on 16 September 1997.

Edwards does not specifically teach a transgenic plant comprising said recombinant polynucleotide.

Harada teaches that at the time of Applicant's invention, it was obvious to transform plants with recombinant polynucleotides encoding CAAT-box transcription factors. Harada teaches a transgenic plant comprising a recombinant nucleotide sequence encoding a LEC1 polypeptide that comprises a CCAAT binding factor domain. Harada teaches that said recombinant nucleotide sequence can be operably linked to a constitutive promoter (claim 7), an inducible promoter (claim 9) or a tissue-specific promoter (claim 11). Harada teaches a method of transforming a plant by selecting a polynucleotide, inserting into an expression vector, introducing said vector into a plant or plant cell and selecting a transformed plant (see column 13, lines 49-58; columns 15-17; and column 20, last paragraph to column 21). Harada teaches that the transgenic plant can be a dicot, a monocot or a gymnosperm (column 21, lines 31-45).

The claims would have been *prima facie* obvious to one of ordinary skill in the art at the time of Applicant's invention, because it would have been obvious to isolate a polynucleotide encoding the complete AtHAP3b gene and transform a plant with the AtHAP3b CAAT-box transcription factor taught by Edwards. The invention as a whole is directed to a transgenic plant. The characteristic of abiotic stress tolerance would have naturally flown from the use of the AtHAP3b CAAT-box transcription factor to transform a wild-type plant. In addition, Edwards teaches that the AtHAP3b CAAT-box transcription factor appears to be expressed in relation to osmotic stress and hence, would have motivated one of ordinary skill in the art to produce a transgenic plant. Hence, it would have been obvious to produce a transgenic plant and select said plant based on a greater tolerance to osmotic stress. Given the success of Harada in making a transgenic plant overexpressing the LEC1 CCAAT-box transcription factor, one of ordinary skill in the art would have had a reasonable expectation of success.

Applicants argue that Edwards states that "[t]he expression of AtHAP3b in leaves from plants grown in soil but not in those from liquid culture may suggest environmental regulation of this gene ... perhaps in relation to osmotic stress.". Applicants argue that the Office suggests that "it would have been obvious to isolate a polynucleotide encoding the complete AtHAP3B gene and transform a plant with the AtHAP3B CAAT-box transcription factor taught by Edwards" and "the characteristic of abiotic stress tolerance would have naturally flown" from the use of the transcription factor (page 6, 5th paragraph of the Remarks).

Applicants argue that this is not the case. Applicants argue that Edwards does not suggest making a transgenic plant overexpressing AtHAP3b, and for good reason. Edwards was published about the same time as Harada et al. and Lotan et al, and as shown below the latter publications teach away from the instant claims and provide a disincentive to combine the references to grow plants that have improved salt or osmotic stress tolerance (said traits would naturally exclude seeds) (page 6, 6th paragraph of the Remarks).

Applicants argue that the accepted wisdom provided by Harada et al. or Lotan et al. (see below) is that LEC1, and homologous sequences that may function together with LEC 1, including HAP3 CCAAT-binding proteins, function at the embryo stage but not beyond. Applicants argue that that one must proceed contrary to this accepted wisdom by combining Harada with the sequences of Edwards is evidence of nonobviousness (page 6, 7th paragraph of the Remarks).

Applicants argue that Harada is a *significant* teaching away from the instant claims since greater salt or osmotic stress tolerance cannot be envisaged if CCAAT-binding proteins, as represented and taught by Harada with LEC 1, are embryo-specific (Harada, col. 1, line 17) and repress the germination process (Harada, col. 27, line 63). Applicants argue that the claimed functions of salt and osmotic stress tolerance are characteristics of plants grown beyond the plant embryo stage. Applicants argue that knowledge that LEC1, which is taught by Harada to be related to HAP3 proteins (e.g., see Harada' s Fig. 2a) is embryo-specific and represses the germination process would direct the skilled artisan away from sequences that are taught to be inoperable with

respect to the instantly claimed traits, including the instant sequences that are, allegedly, sufficiently related to LEC1 to merit an obviousness rejection. Applicants argue that Edwards and Harada, alone or in combination, do not provide a motivation to practice the instantly claimed methods. Applicants argue that immediately after the Harada filing, Lotan et al. Cell (June 26, 1998) 93:1195-1205 (the authors include inventors of 6,235,975 B 1; Lotan was submitted with the IDS of 03-04-2005) also taught that "LEC1 appears to function as a specific regulator of embryo development" (page 1200, col. 1), "LEC1 RNA accumulates only during seed development in embryo cell types and in endosperm" (abstract) since "expression studies showed that the LEC1 gene is active only within seeds during both early and late seed development" (page 1196, col. 1). Applicants argue that when the LEC1 gene was overexpressed, "T1 seeds germinated with an efficiency of only 0.006%, much less than the 1% efficiency typically obtained from *in planta* transformation experiments .... Their roots often did not extend or extended only in sections and sometimes greened" (page 1200, col. 1-2). Applicants argue that Lotan et al. also believe that "the LEC1 polypeptide is homologous to the HAP3 subunit of the CBF class of eukaryotic transcriptional activators that includes NF-Y, CP1, and HAP2/3/4/5" (page 1201, col. 1) and that this "high degree of sequence conservation in the B domain strongly suggests that LEC1 is part of an oligomeric [CCAAT box-binding factor] transcription activator". Applicants argue that Lotan et al. and Harada et al. suggest that LEC1 functions with CCAAT box-binding factors (e.g., instant SEQ ID NO: 2), but the role of LEC1 is only within seeds, and thus cannot confer a role in salt or osmotic stress tolerance. Applicants argue that ectopic expression of

LEC1 produced roots that did not extend or extended only in sections, which would also teach away from improved salt or osmotic stress tolerance since poorly extended roots would be highly unlikely to improve tolerance to these stresses. Applicants argue that given the failure of these authors and inventors to produce healthy plants overexpressing a sequence that was reportedly expressed only in seeds, where the plants have a very poor germination efficiency and poorly extended roots, the combination of Harada and Edwards to produce salt or osmotic stress tolerant plants fails to provide any suggestion or motivation to practice the instantly claimed methods. Applicants argue that it is improper to combine references where the references teach away from their combination. *In re Grasselli*, 713 F.2d 731,743,218 USPQ 769, 779 (Fed. Cir. 1983). Applicants argue that a conclusion of obviousness requires that the reference(s) relied upon be enabling in that it put the public in possession of the claimed invention. *In re Hoeksema*, 399 F.2d 269, 274, 158 USPQ 596, 601 (CCPA 1968) (paragraph spanning pages 6-7 of the Remarks).

These arguments are not found to be persuasive. In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.,* 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). Neither Harada *et al* nor Lotan *et al* teach away from transforming a plant with an AtHAP3b encoding polynucleotide. Lotan *et al* explicitly teaches transforming a plant with a LEC1 encoding polynucleotide at page 1203, right column. The teaching of Lotan *et al* demonstrates a reasonable

expectation of success as T2 plants containing the *35S/LEC1* transgene were grown. Nowhere in the teachings of Edwards *et al* is there a suggestion that the AtHAP3b is involved in embryo development. Edwards *et al* suggests that the AtHAP3b is expressed in leaves from plants grown in soil but not in those from liquid culture (page 1021, left column, 2nd paragraph). Harada *et al* teach what would have been routine experimentation at the time of the instant invention. Edwards *et al* teaches one of ordinary skill in the art what to look for, suggesting that the AtHAP3b is environmentally regulated perhaps in relation to osmotic stress. Consequently, there would have been a limited number of options suggested to one of ordinary skill in the art at the time of Applicants' invention based on the teachings of Edwards *et al*.

Conclusion

7. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

8. No claims are allowed.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to David H. Kruse, Ph.D. whose telephone number is (571) 272-0799. The examiner can normally be reached on Monday to Friday from 8:00 a.m. to 4:30 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anne Marie Grunberg can be reached at (571) 272-0975. The central FAX number for official correspondence is 571-273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group Receptionist whose telephone number is (571) 272-1600.

/David H Kruse/
Primary Examiner, Art Unit 1638